REMARKS

Favorable reconsideration of this application, in light of the preceding amendments and following remarks, is respectfully requested.

Claims 57-61, 71-83, 93-101 and 103 are pending in this application. Claims 57-61, 71-83, 93-101 and 103 are amended and claims 62-70, 84-92, 102 and 104-112 have been cancelled. Claims 57, 60, 81, 83, 100 and 101 are the independent claims.

Applicants note with appreciation the Examiner's acknowledgement that certified copies of all priority documents have been received by the U.S.P.T.O. Action, summary at 12.

Applicants also respectfully note that the present action does not indicate that the drawings have been accepted by the Examiner. Applicants respectfully request that the Examiner's next communication include an indication as to the acceptability of the filed drawings or as to any perceived deficiencies so that the Applicants may have a full and fair opportunity to submit appropriate amendments and/or corrections to the drawings.

Example Embodiments of the Present Application

Independent claim 57 recite a device for promoting regeneration of an injured nerve including a nerve encasement structure, and a plurality of biodegradable guiding fibers, wherein the material of the nerve encasement structure and the material of the guiding fibers each comprises at least one biodegradable polymer, wherein said at least one polymer comprised in the material of the guiding fibers presents an average molecular weight which is

lower than a molecular weight of said at least one polymer comprised in the material of the nerve encasement structure, wherein the material of the nerve encasement structure comprises polyhydroxybutyrate (PHB) and the material of the guiding fibers comprises PHB and the PHB average molecular weight of the nerve encasement structure is within the range of 100,000 to 250,000 daltons and the PHB average molecular weight of the guiding fibers is within the range of 50,000 to < 250,000 daltons, and wherein at least a majority of the guiding fiberspresent an in vivo degradation time (t_1) being less than the time required for establishing regenerated contact between ends of an injured nerve (t_c) using the device for said regeneration. Independent claims 60, 81, 83, 100 and 101 recite similar features.

Example non-limiting embodiments of this feature are discussed, for example, in page 6, lines 26-31 and page 7, line 18 to page 8, line 30 of the instant specification.

As is illustrated in the present application, the difference between the *in vivo* degradation times t1 and t2, and their respective relations to tc and/or tr are responsible for the improved nerve regeneration process achieved. The nerve regeneration process is improved with respect to regeneration time and/or function of the restored nerve.

Claim Objections

Claims 104-112 are objected to because of the following informalities: the status of claims 104-112 is not correct because these claims are withdrawn from consideration. Claims 57-103 are objected to because of the following

informalities: the recitations "t1, tc, t2, tr, PHB, PLGA" recited in claims 57-61, 65-67, 69, 83, 91, 92, 100 and 101 are not a common abbreviation in the art. Applicants are required to spell out "t1, tc, t2, tr, PHB, PLGA" in the first usage. In addition, the Examiner made several suggested amendments to the claims.

Applicants note that appropriate action has been taken to overcome the Examiners objections. Therefore, withdrawal of the objections to claims 57-112 is respectfully requested.

Rejections under 35 U.S.C. § 112, second paragraph

Claims 57-103 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as his invention because the terms "t1, tc, t2 and tr" are received in the claims without a reference to a precise time and claims 58-59, 61-80, 82, 84-99, 102 and 103 because they recite "A device/kit/sheet according to claim x". Applicants respectfully traverse this rejection for the reasons detailed below.

Since the time required for re-established contact between the axon ends, as well as the time required for the nerve to regenerate entirely, is dependent on both the length of the nerve gap and the axon growth rate, Applicants respectfully submit that employing absolute time units for t_1 and t_2 is not appropriate.

However, in the interest of advancing prosecution, all pending claims are amended, where appropriate, to include formula I and/or II, and/or

relationships derived therefrom. As a result, a skilled artisan would readily appreciate what time units are within the definitions of the terms t_1, t_2, t_c and t_r, respectively, for a device intended for a particular nerve gap size. For example, according to amended claim 60, for a nerve gap of 10 mm and estimating the axon growth rate to be 1 mm/day:

- t_r, which is the time required for the entire nerve regeneration, is between 20 and 34 days,
- t_1, which is the in vivo degradation time of the guiding fibers, is always less than t_r, and therefore in this example is always less than 34 days and possibly less than 20 days,
- t_2, which is the in vivo degradation time of the nerve encasement structure, is always longer than t_r and therefore, in this example, always longer than 20 days and also possibly longer than 34 days.

Applicants submit that such calculations, based on simple mathematical relationships and input parameters which either can be directly measured (gap size) or appreciated within a narrow range (axon growth rate) would be obvious to one skilled in the art.

In addition, Applicants have amended all dependent claims to recite "the device/kit/sheet" instead of "a device/kit/sheet".

The Applicants, therefore, respectfully request that the rejection to Claims 57-103 under 35 U.S.C. § 112, second paragraph, be withdrawn.

Rejections under 35 U.S.C. § 112, first paragraph

Claims 57-103 stand rejected under 35 USC 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventor(s), at the time the application was filed, had possession of the claims invention. Applicants respectfully traverse this rejection for the reasons detailed below.

Claims 57, 60, 81, 83, 100 and 101 are amended to comprise "guiding fibers", which is described throughout the specification, in particular, page 7, lines 16-17 of the specification as filed, and in addition, inter alia, the following features:

- the material of the nerve encasement structure/biodegradable sheet/at least one surface and the material of the guiding fibers each comprises at least one biodegradable polymer;
- the at least one polymer comprised in the material of the guiding fibers presents an average molecular weight which is lower than a molecular weight of the at least one polymer comprised in the material of the nerve encasement structure/biodegradable sheet/at least one surface;
- the material of the nerve encasement structure/biodegradable sheet/at least one surface comprises PHB and the material of the guiding fibers comprises PHB; and

- the PHB average molecular weight of the nerve encasement structure/biodegradable sheet/at least one surface is within the range of 100,000 to 250,000 daltons and the PHB average molecular weight of the guiding fibers is within the range of 50,000 to 250,000 daltons.

Also, t_1 and t_2 are defined using their mathematical relationships to t_c and/or t_r. Applicants submit that the present specification clearly discloses devices/kits/biodegradable sheets having the above characteristics. For instance, see the Example (pages 26 – 27 of the specification as filed) for the construction of nerve conduits from nonwoven sheets of polyhydroxybutyrate (PHB) and non-bonded PHB fibers, and Table 1 for examples of t_1 and t_2.

Applicants thus respectfully submit that the claims as amended encompass only what is described in the present specification and/or what a person skilled in the art would readily understand from the specification using prior art teachings and his general knowledge of the field.

The Applicants, therefore, respectfully request that the rejection to Claims 57-103 under 35 U.S.C. § 112, first paragraph, be withdrawn.

Rejections under 35 U.S.C. § 102

Williams et al. as evidenced by Seckel and Chlavijo-Alvarez et al.

Claims 57-67, 71-74, 77-89, 93-97 and 100-103 stand rejected under 35 U.S.C. § 102(b) as being anticipated by US Patent No. 6,548,569 (Williams et al.) hereinafter "Williams" as evidenced by US Patent No. 5,584,885 (Seckel) hereinafter "Seckel" and Plast. Reconstr. Surg. 2007. 119:1939-1851 (Chlavijo-

Alvarez et al.), hereinafter "Chlavijo-Alvarez". Applicants respectfully traverse this rejection for the reasons detailed below.

In view of the above amendments to the claims, Applicants respectfully submit that Williams does not anticipate the subject matter of independent claims 57, 60, 81, 83, 100 and 101. In particular, Williams does not disclose a device/kit/biodegradable sheet/ comprising biodegradable guiding fibers wherein said at least one polymer comprised in the material of the guiding fibers presents an average molecular weight which is lower than a molecular weight of said at least one polymer comprised in the material of the nerve encasement structure/sheet/at least one surface as recited in independent claims 57, 60, 81, 83, 100 and 101.

Furthermore, since the guiding fibers of the device of Williams do not specifically have an average molecular weight that is lower than that of the encasement structure, the device of Williams would not necessarily have the same properties as provided by t_1, t_2, t_c and t_r as recited in independent claims 57, 60, 81, 83, 100 and 101.

Neither Seckel or Clavijo-Alvarez disclose a nerve conduit including a nerve encasement structure which comprises PHB and guiding fibers also comprising PHB. Thus, neither Seckel or Clavijo-Alvarez does not anticipate independent claims 57, 60, 81, 83, 100 and 101 as amended.

Claims 62-67, 84-89 and 102 have been cancelled, and therefore, the rejection of these claims is now moot.

The Applicants, therefore, respectfully request that the rejection to Claims 57, 60, 81, 83, 100 and 101 under 35 U.S.C. § 102(b) be withdrawn.

Claims 58, 59, 61, 71-74, 77-82, 93-97 and 103, dependent on independent claims 57, 60, 81, 83, 100 and 101, are patentable for the reasons stated above with respect to claims 57, 60, 81, 83, 100 and 101 as well as for their own merits.

Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection to independent claims 57, 60, 81, 83, 100 and 101 and all claims dependent thereon.

Rejections under 35 U.S.C. § 103

Williams et al. in view of Hansson et al. and Seckel

Claims 57-103 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over US Patent No. 6,548,569 (Williams et al.) hereinafter "Williams" in view of US Patent No. 5,656,605 (Hansson et al.), hereinafter "Hansson" and US Patent No. 5,584,885 (Seckel) hereinafter "Seckel". Applicants respectfully traverse this rejection for the reasons detailed below.

Applicants respectfully submit that it would **not** have been obvious to one of ordinary skill in the art at the time the invention was made to employ guiding fibers having a molecular weight lower than that of the encasement structure, as suggested by the Examiner. Applicants submit that the cited art does not teach the use of nerve conduit structures of the same polymeric material but of different molecular weights, or the use of guiding fibers which degrade more quickly than the encasement. Applicants further submit that it would not have been obvious for a person of ordinary skill in the art at the time

the invention was made to differentiate the PHB molecular weights of the different conduit structures to tailor to different in vivo degradation times.

Further, Applicants submit that there is no suggestion in the cited art that a material of low molecular weight degrading more quickly than the corresponding material of high molecular weight under identical conditions is desirable. Williams merely teaches that the molecular weight of the PHB used for a nerve guide may be chosen from the range of 10,000 to 10,000,000 Da. Hence, in view of the cited art, the person of ordinary skill in the art would have no motivation to use a nerve regeneration device with guiding fibers having a molecular weight lower than that of the encasement. Moreover, in case the degradation rate of the conduit is to be altered, Williams explicitly teaches the use of additives, pendant groups, chemical modifications (e.g. including chemical linkages which are more susceptible to hydrolysis or enzymatic attack), and processing techniques such as moulding or lamination.

Since biodegradation of nerve conduits is typically caused by ingrowth of blood vessels and cell invasion (Jansen K, van der Werff JF, van Wachem PB, Nicolai JP, de Leij LF, van Luyn MJ (2004) Biomaterials 25: 483-489), using a nerve conduit having an encasement and guiding fibers of the same material and of the same molecular weight would result in the encasement structure being degraded in vivo before the guiding fibers, because the guiding fibers would not be sufficiently exposed to such degrading factors until the encasement is essentially disintegrated (that is, initially the conditions within the encasement are not identical to those outside the encasement). However, where the molecular weight of the guiding fibers is lower than that of the

encasement, as is the case in the independent claims of the present invention, there is a much lesser degree of disintegration of the encasement (i.e., the encasement not being essentially disintegrated is sufficient to provide a degrading environment for the guiding fibers).

Therefore, Applicants respectfully submit that neither Williams, Hansson, Seckel, nor the combination thereof would render independent claims 57, 60, 81, 83, 100 and 101 obvious.

Claims 62-70, 84-92 and 102 have been cancelled, and therefore, the rejection of these claims is now moot.

The Applicants, therefore, respectfully request that the rejection to Claims 57, 60, 81, 83, 100 and 101 under 35 U.S.C. § 103(a) be withdrawn.

Claims 56, 58-59, 61-80, 82, 84-99, 102 and 103, dependent on independent claims 57, 60, 81, 83, 100 and 101, are patentable for the reasons stated above with respect to claims 57, 60, 81, 83, 100 and 101 as well as for their own merits.

Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection to independent claims 57, 60, 81, 83, 100 and 101 and all claims dependent thereon.

CONCLUSION

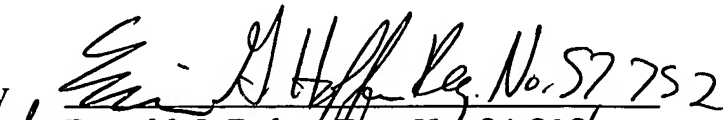
In view of the above remarks and amendments, the Applicants respectfully submit that each of the pending objections and rejections has been addressed and overcome, placing the present application in condition for allowance. A notice to that effect is respectfully requested. If the Examiner believes that personal communication will expedite prosecution of this application, the Examiner is invited to contact the undersigned.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Erin G. Hoffman, Reg. No. 57,752, at the telephone number of the undersigned below.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 08-0750 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17; particularly, extension of time fees.

Respectfully submitted,

HARNESS, DICKEY, & PIERCE, P.L.C.

By 
Donald J. Daley, Reg. No. 34,313
P.O. Box 8910
Reston, Virginia 20195
(703) 668-8000

DJD/EGH/dmc/ljs